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NOTICE OF ALLOWANCE AND FEE(S) DUE

959 7590 06/18/2008

LAHIVE & COCKFIELD, LLP
ONE POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/18/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,353	11/14/2003	Janine Schuurman	GMI-059	6363

TITLE OF INVENTION: HUMAN MONOCLONAL ANTIBODIES AGAINST CD25

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1440	$300	$0	$1740	09/18/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

959 7590 06/18/2008

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

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10/714,353	11/14/2003	Janine Schuurman	GMI-059	6363

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nonprovisional	NO	$1440	$300	$0	$1740	09/18/2008

EXAMINER	ART UNIT	CLASS-SUBCLASS
BRISTOL, LYNN ANNE	1643	424-133100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☐ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 384 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 384 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	10/714,353	SCHUURMAN ET AL.	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the response of 2/28/08*.

2. ☒ The allowed claim(s) is/are *2-11, 13, 15, 17, 19-21, 53-55, 67, 99-102 and 109-115*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____.
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/David J Blanchard/
Primary Examiner, Art Unit 1643

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/28/08 has been entered.

2. Claims 2-11, 13, 15, 17, 19-21, 53-55, 67, 99-102 and 109-115 are all the pending claims for this application.

3. Claims 40-50 were cancelled, Claim 17 was amended and new Claims 109-115 were added in the Response of 2/28/08. Claim 56 is cancelled by Examiner's Amendment as discussed below.

4. Claims 2-11, 13, 15, 17, 19-21, 53-55, 67, 99-102 and 109-115 are all the claims under examination.

Withdrawal of Objections

5. The objection to Claim 17 for being inconsistent with Claims 11, 13 and 15 is withdrawn in view of the amendment of Claim 17 to recite "which binds to human CD25". Applicants' comments in the middle of p. 8 of the Response of 2/28/08 are acknowledged.

Withdrawal of Rejections

Claim Rejections - 35 USC § 112, first paragraph

Enablement

6. The rejection of Claims 2, 4, 40-50, 53 and 54 under 35 U.S.C. 112, first paragraph, in lacking enablement for a) making or expressing any human anti-human CD25 antibody from a XenoMouse animal and b) making any conservative amino acid substitutions within CDRs that do not effect antibody binding is withdrawn as set forth below.

a) For purposes of review, the rejection of Claims 2, 4, 53 and 54 from the Office Action of 11/2/07 is set forth below:

"Claims 2, 4, 53 and 54 are directed to antibodies comprising the isotype of IgG2, IgG3, IgG4, IgM, IgA1, IgA2, secretory IgG, IgD or IgE. The same rejection was raised against these claims in the Office Action of 5/21/07.

Applicants have identified and characterized *only* four (4) anti-human CD25 antibody clones (AB1, AB7, AB11 and AB12) expressed from the germline gene sequence from HCo mice ((CMD)++; (HCo7) 11952+; (JKD) ++; (KCo5) 9272+ genotype) and ***all were IgG1, kappa*** (p. 56, lines 7-11).

As discussed in the Office Action of 5/21/07, Davis et al. ((1999) Can. Metastasis Rev. 18:421-425; cited in the PTO 892 form of 5/21/07) describes neutralizing antibodies for epidermal growth factor receptor produced from XenoMouse animals shared similar gene composition and out 8 clones each shared one of 2 VH genes (Table 3). Davis teaches "there appear to be rigorous structural requirements for antibodies that bind effectively to the ligand binding site on EGFr" (p. 425, Col. 1).

As discussed in the Office Action of 5/21/07, Gallo et al. (Eur. J. Immunol. (2000) 30:534-540; cited in the PTO form 892 of 5/21/07) compared XenoMouse and human VH gene segment usage for the VH3 and VH4 gene segments and found the same genes to utilized and to the same degree, thus the VH gene segmentation representation in the XenoMouse repertoire appears to be substantially the same as observed in humans (Figures 1 and 2). Similar findings were reported for JH gene segments between human and XenoMouse repertoires (Table 3).

Thus one skilled in the art could not have practiced or would have expected to obtain any Ig class of human anti-CD25 antibody having structural diversity from a transgenic mouse and meeting all the functional properties for a human CD25 antibody as broadly encompassed by the claims."

Applicants' allegations on pp. 9-10 of the Response of 2/28/08 and the four (4) literature references relied on in the arguments have carefully considered and are found persuasive.

Applicants allege that "once provided with the variable region sequence information (as claimed), antibodies of varying classes could have been produced

without undue experimentation by recombinant technology", the specification at p. 23, lines 18-23 support inserting the VH and VL segments into vectors, and expression vectors for expressing different antibody isotypes are disclosed (pp. 27-28), and methods of generating antibodies having different isotypes were already known in the art, where Applicants cite the following references as evidence for cloning variable domains into different antibody isotopes existed at the time of filing:

Preston et al. (Infect. Immun. 66(9):4137-4142 (1998))

Yarnold and Fell (Can. Res. 54:506-512 (1994))

Morrison et al. (PNAS 88:6851-6855 (1994))

Boel et al. (J. Immunol. Methods 239:153-166 (2000)).

b) The rejection of Claims 40-50 in lacking enablement for making any conservative amino acid substitutions within CDRs without effecting antibody binding is withdrawn and moot for the cancelled claims.

EXAMINER'S AMENDMENT

7. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jeanne DiGiorgio on 5/16/08 and 5/20/08. The claims are amended as follows:

5. (currently amended) The antibody of any one of claims 99-102, wherein the antibody dissociates from human CD25 with a dissociation equilibrium constant (K_D) of

10^{-8} M or less, ~~preferably of about 10^{-9} M or less, and more preferably of about 10^{-10} M or less, or 10^{-11} M or even less,~~ when determined by surface plasmon resonance (SPR) technology in a BIAcore 3000 instrument using human recombinant CD25 as the ligand and the antibody as the analyte.

19. (currently amended) An isolated monoclonal antibody that binds human CD25, comprising a full heavy chain and a full light chain variable region, wherein at least one human variable region is selected from the group consisting of: SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, and 16.

54. (currently amended) The antibody of any one of claims 99-102, which is an intact antibody selected from the group consisting of an intact IgG1, κ antibody; an intact IgG1, λ antibody; an intact IgG4, κ antibody; and an intact IgG4, λ antibody, wherein the antibody is glycosylated in a eukaryotic cell.

56. (cancelled)

115. (currently amended) An isolated monoclonal antibody that binds human CD25, comprising a full heavy chain and a full light chain variable region, wherein at least one variable region is selected from the group consisting of: SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, and 16.

Examiner's Statement of Reasons for Allowance

8. The following is an examiner's statement of reasons for allowance: the claimed antibodies directed to variable regions and corresponding respective CDRs of the anti-

CD25 monoclonal antibodies disclosed in the specification, are found to be novel, non-obvious and enabled.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

9. Claims 2-11, 13, 15, 17, 19-21, 53-55, 67, 99-102 and 109-115 are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

/David J Blanchard/
Primary Examiner, Art Unit 1643